Fiscal Year:	FY 2015	**Task Last Updated:**	FY 08/02/2014
PI Name:	Wang, Huichen		
Project Title:	Molecular Basis of DNA Repair and Protection from Apoptosis in Neuronal Progenitors Exposed to Space Radiation		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **SR**:Space Radiation		
Human Research Program Risks:	(1) **BMed**:Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
PI Email:	huwang@pvamu.edu	**Fax:**	FY
PI Organization Type:	UNIVERSITY	**Phone:**	936-261-3156
Organization Name:	Prairie View A & M University		
PI Address 1:	P.O. Box 519 MS2230		
PI Address 2:	New Science Bldg 322		
PI Web Page:			
City:	Prairie View	**State:**	TX
Zip Code:	77446	**Congressional District:**	10
Comments:	Formerly at Emory University, relocated in September 2014 (Ed., 7/7/15)		
Project Type:	GROUND	**Solicitation / Funding Source:**	2008 Space Radiobiology NNJ08ZSA001N
Start Date:	10/01/2008	**End Date:**	10/01/2014
No. of Post Docs:	1	**No. of PhD Degrees:**	1
No. of PhD Candidates:		**No. of Master' Degrees:**	
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:		**Monitoring Center:**	NASA JSC
Contact Monitor:	Simonsen, Lisa	**Contact Phone:**	
Contact Email:	lisa.c.simonsen@nasa.gov		
Flight Program:			
Flight Assignment:	NOTE: End date is 9/19/2014 (changed from 9/30/2015) per PI move; setting end date to 10/1/14 for reporting purposes (Ed., 7/7/15) NOTE: End date is now 9/30/2015 per NSSC information (Ed., 7/11/14) NOTE: End date is now 9/30/2014 per PI and NSSC information (Ed., 8/3/2013) NOTE: End date is now 9/30/2013 per NSSC information (Ed., 3/12/2013) NOTE: Extended to 3/31/2013 per NSSC information (Ed., 12/18/12)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Krzysztof, Reiss (Neurological Cancer Research, Stanley S. Scott Cancer Center, Louisiana State University Health. Sciences Center, New Orleans, LA)		
Grant/Contract No.:	NNX08BA08G		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	The health risks to astronauts exposed to space radiation include cognitive deficits and possibly accelerated aging. While the pathogenesis of radiation-induced cognitive dysfunction remains largely uncharacterized, it is thought to include loss of neural progenitors from the brain. Understanding of the molecular and cellular bases underlying neuronal loss and/or dysfunction is absolutely required for the development of countermeasures before, during and possibly after space missions. Since experiments in humans are not possible, studies in this direction will benefit from appropriate biological model systems. The neurodegenerative effects of space radiation are likely to derive from DNA damage in the central nervous system (CNS). Therefore, research involving repair of this type of DNA lesions is critical for the development of new neuroprotective countermeasures. In the present proposal, we introduce an in vitro model of neural progenitors (neurospheres), which is derive from the brain of mouse embryo from neurodegenerative transgenic mice to study the detrimental effects of space radiation at the mechanistic level. Using this biological model, we will study DNA damage repair and apoptosis of proliferating and differentiated neural progenitor exposed to low dose of high charge and energy nuclei and protons. The proposed studies will provide novel insights into the molecular and cellular mechanisms underlying CNS risks from space radiation and will help to predict and countermeasure health risks from space radiation particularly with regard to effects on the CNS.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	This proposal will study the mechanism of DNA damage and oxidative stress in neuronal cells induced by high energy particle, iron, and protons, compared to X-ray. This study will provide possible ways to develop accurate quantitative estimates to the risk of the central nervous system (CNS) from galactic cosmic ray (GCR) and solar particles events following long-term space travel.
Task Progress:	High linear energy transfer (LET) radiation induces clustered DNA damage and delayed oxidative stress which prolongs their response signaling to the progeny of irradiated cells, leading to alteration of homeostasis, including cell death program (apoptosis, autophagy, and senescence) and cell growth. Here we investigated the molecular and cellular mechanism of persistent DNA damage response, cell survival, and cell death of hippocampal neuronal cells following exposure to heavy ion particles and proton. We found that DNA damage response signaling persists longer in hippocampal neuronal cells exposed to high LET radiation (56Fe (1Gev/n)) than to low LET radiation (proton (1Gev/n)). High LET radiation induced higher phosphorylation of Tip60, expression of p53, p21, and PUMA than low LET radiation. GSK3 inhibitors reduced Tip60 phosphoryaltion, p53, and PUMA expression. Inhibition of GSK3 activity reduced the cell killing of hippocampal neuronal cells following exposure to high LET radiation. High LET radiation induced more apoptosis, senescence, and autophagy than low LET radiation. This suggests that high LET radiation may sustain DNA damage signaling and change cellular homeostasis of energy and growth, implying the risk to the central nervous system (CNS). ED. NOTE (7/7/15): Project continues as "Molecular Basis of DNA Repair and Protection from Apoptosis in Neuronal Progenitors Exposed to Space Radiation" grant NNX14AT39G, due to PI move to Prairie View A&M University in September 2014.
Bibliography Type:	Description: (Last Updated: 11/13/2019)
Abstracts for Journals and Proceedings	Kandimalla R, Tang X, Wang T, Wang H. "High LET radiation produces sustained DNA damaging signaling and change cellular homestasis in hippocampal neuronal cells." Presented at 2014 NASA Human Research Program Investigators' Workshop, Galveston, TX, February 12-13, 2014. 2014 NASA Human Research Program Investigators' Workshop, Galveston, TX, February 12-13, 2014. http://www.hou.usra.edu/meetings/hrp2014/pdf/3306.pdf , Feb-2014
Abstracts for Journals and Proceedings	Werner E, Tang X, Wang H, Doetsch P. "The role of persistent phenotype in radiation-induced genomic instability." 2014 NASA Human Research Program Investigators' Workshop, Galveston, TX, February 12-13, 2014. 2014 NASA Human Research Program Investigators' Workshop, Galveston, TX, February 12-13, 2014. http://www.hou.usra.edu/meetings/hrp2014/pdf/3187.pdf , Feb-2014
Abstracts for Journals and Proceedings	Werner E, Kandimalla R, Wang H, Doetsch P. "A role for reactive oxygen species in the resolution of persistent genomic instability after exposure to radiation." 6th International Workshop on Space Radiation Research, Chiba, Japan, 15-18 May 2013. Journal of Radiation Research (Impact Factor: 1.45). 2014 Mar;55(Suppl 1):i14. http://dx.doi.org/10.1093/jrr/rrt183 , Mar-2014